

WHAT IS CLAIMED IS:

1. A human glycoprotein hormone family protein comprising at least one electrostatic charge altering mutation in a  $\beta$  hairpin loop structure, wherein said mutation results in said human glycoprotein hormone family protein having increased bioactivity.

5 2. The human glycoprotein hormone family protein of Claim 1, wherein the protein is the human chorionic gonadotropin (CG)  $\beta$  subunit.

3. The human glycoprotein hormone family protein of Claim 2, wherein the at least one electrostatic charge altering mutation is in the L1  $\beta$  hairpin loop at a position selected from the group consisting of positions 1-37.

10 4. The human glycoprotein hormone family protein of Claim 3, wherein the at least one electrostatic charge altering mutation comprises at least one basic residue introducing mutation selected from the group consisting of S1B, P4B, L5B, P7B, R8B, R10B, P11B, I12B, N13B, A14B, T15B, L16B, A17B, V18B, G22B, P24B, V25B, I27B, T28B, V29B, N30B, T31B, T32B, I33B, A35B, G36B, and Y37B, wherein B is a basic amino acid residue.

15 5. The human glycoprotein hormone family protein of Claim 2, wherein the at least one electrostatic charge altering mutation is in the L3  $\beta$  hairpin loop at a position selected from the group consisting of positions 58-87.

20 6. The human glycoprotein hormone family protein of Claim 5, wherein the at least one electrostatic charge altering mutation comprises at least one basic residue introducing mutation selected from the group consisting of N58B, Y59B, V62B, F64B, S66B, I67B, L69B, P70B, G71B, P73B, G75B, V76B, N77B, P78B, G79B, V80B, S81B, Y82B, A83B, V84B, A85B, L86B, and S87B, wherein B is a basic amino acid residue.

25 7. The human glycoprotein hormone family protein of Claim 2, wherein the subunit is linked to another cystine knot growth factor monomer.

8. The human glycoprotein hormone family protein of Claim 1, wherein the protein is the human luteinizing hormone (LH)  $\beta$  subunit.

9. The human glycoprotein hormone family protein of Claim 8, wherein the at least one electrostatic charge altering mutation is in the L1  $\beta$  hairpin loop at a position selected from the group consisting of positions 1-33.

30 10. The human glycoprotein hormone family protein of Claim 9, wherein the at least one electrostatic charge altering mutation comprises at least one basic residue introducing

mutation selected from the group consisting of W8B, P11B, I12B, N13B, A14B, I15B, L16B, A17B, V18B, G22B, P24B, V25B, I27B, T28B, V29B, N30B, T31B, T32B, and I33B, wherein B is a basic amino acid residue.

11. The human glycoprotein hormone family protein of Claim 8, wherein the at least one electrostatic charge altering mutation is in the L3  $\beta$  hairpin loop at a position selected from the group consisting of positions 58-87.

12. The human glycoprotein hormone family protein of Claim 8, wherein the at least one electrostatic charge altering mutation comprises at least one basic residue introducing mutation selected from the group consisting of N58B, Y59B, V62B, F64B, S66B, I67B, L69B, P70B, G71B, P73B, G75B, V76B, N77B, P78B, G79B, V79B, V80B, S81B, Y82B, A83B, V84B, A85B, L86B, and S87B, wherein B is a basic amino acid residue.

13. The human glycoprotein hormone family protein of Claim 8, wherein the subunit is linked to another cystine knot growth factor monomer.

14. The human glycoprotein hormone family protein of Claim 1, wherein the protein is the human follicle stimulating hormone (FSH)  $\beta$  subunit.

15. The human glycoprotein hormone family protein of Claim 14, wherein the at least one electrostatic charge altering mutation is in the L1  $\beta$  hairpin loop at a position selected from the group consisting of positions 4-27.

16. The human glycoprotein hormone family protein of Claim 15, wherein the at least one electrostatic charge altering mutation comprises at least one basic residue introducing mutation selected from the group consisting of I5B, T6B, N7B, I8B, T9B, I10B, A11B, I12B, F19B, I21B, S22B, I23B, N24B, T25B, T26B, and W27B, wherein B is a basic amino acid residue.

17. The human glycoprotein hormone family protein of Claim 14, wherein the at least one electrostatic charge altering mutation is in the L3  $\beta$  hairpin loop at a position selected from the group consisting of positions 65-81.

18. The human glycoprotein hormone family protein of Claim 17, wherein the at least one electrostatic charge altering mutation comprises at least one basic residue introducing mutation selected from the group consisting of A65B, A68B, S70B, L71B, Y72B, T73B, Y74B, P75B, V76B, A77B, T78B, and Q79B, wherein B is a basic amino acid residue.

add  $a^5$

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